Claims

1. A method for diagnosing or prognosticating age-related macular degeneration in a subject, or determining whether a subject is at increased risk of developing age-related macular degeneration, comprising:
determining a level, or an activity, or both said level and said activity, of at least one substance which is selected from the group consisting of a transcription product of a Cystatin C gene, a translation product of a Cystatin C gene, a fragment of said translation product, an amyloid protein, and a transcription product of a gene coding for an amyloid protein in a sample from said subject;
and
comparing said level, or said activity, or both said level and said activity, of at least one of said substances to a reference value representing a known disease or health status,
thereby diagnosing or prognosticating said age-related macular degeneration in said subject, or determining whether said subject is at increased risk of developing age-related macular degeneration.

2. A method of monitoring the progression of age-related macular degeneration in a subject, comprising:
determining a level, or an activity, or both said level and said activity, of at least one substance which is selected from the group consisting of a transcription product of a Cystatin C gene, a translation product of a Cystatin C gene, a fragment of said translation product, an amyloid protein, and a transcription product of a gene coding for an amyloid protein in a sample from said subject;
and

comparing said level, or said activity, or both said level and said activity, of at least one of said substances to a reference value representing a known disease or health status,
thereby monitoring the progression of said age-related macular degeneration in said subject.

3. A method of evaluating a treatment for age-related macular degeneration, comprising:
determining a level, or an activity, or both said level and said activity, of at least one substance which is selected from the group consisting of a transcription product of a Cystatin C gene, a translation product of a Cystatin C gene, a fragment of said translation product, an amyloid protein, and a transcription product of a gene coding for an amyloid protein, in a sample obtained from a subject being treated for said age-related macular degeneration;
and
comparing said level, or said activity, or both said level and said activity, of at least one of said substances to a reference value representing a known disease or health status,
thereby evaluating said treatment for said age-related macular degeneration.

4. The method according to at least one of claims 1 to 3, wherein said sample is taken from a body fluid, a tissue, or an organ, in particular an eye, of said subject.

5. The method according to claim 4, wherein said sample is taken from material located between the plasma membrane and basal lamina of the retinal pigment epithelium.

6. The method according to claim 4, wherein said sample is taken from material located between the basal lamina of the retinal pigment epithelium and the inner collagenous zone of Bruch's membrane.

7. The method according to at least one of claims 1 to 6, wherein a variation of said level of Cystatin C or a transcription product of a Cystatin C gene in said sample from said subject relative to said reference value representing a known health status indicates a diagnosis, or prognosis, or increased risk of said age-related macular degeneration in said subject.

8. The method according to at least one of claims 1 to 7, wherein a varied activity of Cystatin C in said sample from said subject relative to said reference value representing a known health status indicates a diagnosis, or prognosis, or increased risk of said age-related macular degeneration in said subject.

9. The method according to at least one of claims 1 to 8, wherein said Cystatin C gene is a polymorphic variant of the Cystatin C wild-type gene.

10. The method according to claim 9, wherein the presence of at least one B allele indicates said subject is at increased risk of developing age-related macular degeneration or indicates a diagnosis or prognosis of age-related macular degeneration.

11. The method according to claim 10, wherein the presence of the B/B genotype indicates said subject is at increased risk of developing age-related macular degeneration or indicates a diagnosis or prognosis of age-related macular degeneration.

12. The method according to at least one of claims 1 to 11, wherein said subject is a human.

13. The method according to at least one of claims 1 to 12, wherein said Cystatin C is determined in its monomeric form.

14. The method according to at least one of claims 1 to 13, wherein at least one of said substances is detected using an immunoassay, an enzyme activity assay and/or a binding assay.

15. The method according to at least one of claims 1 to 14, wherein said reference value is that of a level, or an activity, or both said level and said activity, of at least one substance which is selected from the group consisting of a transcription product of a Cystatin C gene, a translation product of a Cystatin C gene, a fragment of said translation product, an amyloid protein, and a transcription product of a gene coding for an amyloid protein in a sample from a subject not suffering from said age-related macular degeneration.

16. The method according to at least one of claims 1 to 15, further comprising comparing a level, or an activity, or both said level and said activity, of at least one substance which is selected from the group consisting of a transcription product of a Cystatin C gene, a translation product of a Cystatin C gene, a fragment of said translation product, an amyloid protein, a transcription product of a gene coding for an amyloid protein in said sample with a level, an activity, or both said level level and said activity, of at least one of said substances in a series of samples taken from said subject over a period of time.

17. The method according to at least one of claims 1 to 16, wherein said subject receives a treatment prior to one or more of said sample gatherings.

18. The method according to claim 17, wherein said level, or said activity, or both said level and said activity, in said samples is determined, before and after said treatment is administered to said subject.

19. A method of diagnosing or prognosticating age-related macular degeneration in a subject, or determining whether a subject is at increased risk of developing age-related macular degeneration comprising:
determining a presence or absence of a mutation or polymorphism in a Cystatin C gene in a sample from said subject,
thereby diagnosing or prognosticating age-related macular degeneration in said subject, or determining whether said subject is at increased risk of developing age-related macular degeneration.

20. The method of claim 19, wherein the presence or absence of at least one B allele is determined.

21. The method of claim 20, wherein the presence of at least one B allele, in particular the presence of the B/B genotype, indicates said subject is at increased risk of developing age-related macular degeneration or indicates a diagnosis or prognosis of age-related macular degeneration.

22. The method of at least one of claims 19 to 21, further comprising:
determining a level, or an activity, or both said level and said activity, of at least one substance which is selected from the group consisting of a transcription product of a Cystatin C gene, a translation product of a Cystatin C gene, a fragment of said translation product, an amyloid protein, and a transcription product of a gene coding for an amyloid protein, in a sample from said subject;
and

comparing said level, or said activity, or both said level and said activity, of at least one of said substances to a reference value representing a known disease or health status.

23. The method according to claim 22, wherein a variation of said level of Cystatin C or a transcription product of a Cystatin C gene in said sample from said subject relative to said reference value representing a known health status indicates a diagnosis, or prognosis, or increased risk of said age-related macular degeneration in said subject.

24. The method according to claim 22 or 23, wherein a varied activity of Cystatin C in said sample from said subject relative to said reference value representing a known health status indicates a diagnosis, or prognosis, or increased risk of said age-related macular degeneration in said subject.

25. Use of a kit for diagnosis or prognosis of age-related macular degeneration, or for determination of increased risk of developing age-related macular degeneration, or for monitoring progression of age-related macular degeneration in said subject, or for monitoring success or failure of a therapeutic treatment of said subject, said kit comprising at least one reagent which is selected from the group consisting of (i) reagents that selectively detect a transcription product and/or a translation product of a Cystatin C gene, (ii) reagents that selectively detect a fragment of a translation product of a Cystatin C gene, (iii) reagents that selectively detect a mutation or polymorphism in a Cystatin C gene, and (iv) reagents that selectively detect a transcription product and/or a translation product of a gene coding for an amyloid protein.

26. The use according to claim 25 wherein said reagents selectively detect a polymorphic variant of the wild-type Cystatin C gene.

27. The use according to claim 26 wherein said reagents selectively detect a B allele of the Cystatin C gene.

28. The use according to at least one of claims 25 to 27 for working the methods according to claims 1 to 24.

29. A method of treating or preventing age-related macular degeneration in a subject comprising administering to said subject in a therapeutically effective amount an agent or agents which modulate(s) an activity, or level, or both said activity and level, of at least one substance which is selected from the group consisting of a Cystatin C gene, a transcription product of a Cystatin C gene, a translation product of a Cystatin C gene, a fragment of said translation product, a gene coding for an amyloid protein, a transcription product of a gene coding for an amyloid protein, and an amyloid protein.

30. The method according to claim 29 wherein said agent(s) modulate the activity and/or level of (i) a polymorphic variant of the wild-type Cystatin C gene, and/or (ii) a transcription product of (i), and/or (iii) a fragmented or unfragmented translation product of (i),

31. The method according to claim 29 or 30, wherein said agents are cathepsin derivatives or Cystatin C analoga.

32. The method according to at least one of claims 29 to 31, wherein per se known methods of gene therapy and/or antisense nucleic acid technology are applied to administer said agent(s).

33. The method according to at least one of claims 29 to 32 comprising grafting donor cells into the eye of said subject, said subject or donor cells preferably treated so as to minimise or reduce graft rejection,

wherein said donor cells are genetically modified by insertion of at least one transgene encoding said agent(s).

34. A modulator of an activity, or level, or both said activity and level, of at least one substance which is selected from the group consisting of a Cystatin C gene, a transcription product of a Cystatin C gene, a translation product of a Cystatin C gene, a fragment of said translation product, a gene coding for an amyloid protein, a transcription product of a gene coding for an amyloid protein, and an amyloid protein.

35. A medicament comprising a modulator according to claim 34.

36. A modulator of an activity, or level, or both said activity and level, of at least one substance which is selected from the group consisting of a Cystatin C gene, a transcription product of a Cystatin C gene, a translation product of a Cystatin C gene, a fragment of said translation product, a gene coding for an amyloid protein, a transcription product of a gene coding for an amyloid protein, and an amyloid protein, for treating or preventing age-related macular degeneration.

37. The modulator of claims 34 or 36, wherein the modulator is capable of modulating a polymorphic variant of the wild-type Cystatin C gene, in particular a B allele.

38. Use of a modulator of an activity, or level, or both said activity and level, of at least one substance which is selected from the group consisting of a Cystatin C gene, a transcription product of a Cystatin C gene, a translation product of a Cystatin C gene, a fragment of said translation product, a gene coding for an amyloid protein, a transcription product of a gene coding for an amyloid protein, an amyloid protein, for a preparation of a medicament for treating or preventing age-related macular degeneration.

39. A method for identifying pharmaceutical modulators of age-related macular degeneration, comprising the steps of:

- providing a sample containing at least one substance which is selected from the group consisting of a Cystatin C gene, a transcription product of a Cystatin C gene, a translation product of a Cystatin C gene, a fragment of said translation product, a gene coding for an amyloid protein, a transcription product of a gene coding for an amyloid protein, and an amyloid protein;
- contacting said sample with at least one agent; and
- comparing an activity, or level, or both said activity and level, of at least one of said substances before and after said contacting.

40. The method according to claim 39, wherein comparing an activity of Cystatin C is performed by using amyloid precursor protein as a substrate and a generation of A-beta peptides as a read-out.